PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PAC/eehc/22013WO	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/GB2004/004605	International filing date *(day/month/year)* 01.11.2004	Priority date *(day/month/year)* 30.10.2003
International Patent Classification (IPC) or national classification and IPC INV. A61K9/42		
Applicant CIPLA LIMITED et al		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of 15 sheets, as follows:
      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

- ☒ Box No. I Basis of the report
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
03.02.2006	01.06.2006
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized officer Epskamp, S Telephone No. +31 70 340-2857

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/GB2004/004605

Box No. I Basis of the report

1. With regard to the **language**, this report is based on

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3(a) and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4(a))
   - ☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a))

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

   Description, Pages

   1-18 as originally filed

   Claims, Numbers

   1-85 filed with telefax on 02.03.2006

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 78-80 with respect to industrial applicability

because:

☒ the said international application, or the said claims Nos. 78-80 with respect to industrial applicability relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed *(specify)*.

☐ no international search report has been established for the said claims Nos.

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13*ter*.1(a) or (b) and 13*ter*.2.

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions, and such tables were not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-85
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-85
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-77, 81-85
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 78-80 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:
D1: US 2003/0180352 A
D2: WO 01/37816 A
D3: EP 0 503 440 A
D4: WO 02/09675 A

Clarity

1 - In independent claims 1, 42, 60, 78, 81 and 84 an attempt is made to define a compound by its activity: "5-HT receptor agonist".
Such claims, in which an active agent is characterized by its activity, can only be clear if instructions, in the form of experimental tests or any testable criteria, are available from the patent documents or from the general knowledge allowing the skilled person to recognise which active agents fall within the functional definition, i.e. the activity, and accordingly within the scope of the claim. Since such instructions are not provided, the concept "5-HT receptor agonist" is not clear.
Furthermore, the concept of a "derivative" (claims 1, 42, 60 and a number of dependent claims) is vague and unclear, and does not allow the reader to determine the scope of protection sought
Consequently, the subject-matter of claim 1, 42, 60, 78, 81 and 84 is not clear (Art 6 PCT).

Novelty

2 - Claims 1-85, as far as clear, are considered novel (Article 33(2) PCT). Documents D1-D4 show coated compositions comprising sumatriptan (D1-D3) or eletriptan (D4), but no compositions are disclosed comprising these active agents and a coating comprising

waxes.

Inventive Step

3 - Claims 1-85, as far as clear, are also considered inventive (Article 33(3) PCT).

4 - D1 is considered the closest state of the art. It discloses pellets comprising sumatriptan, seal coated with PVP or Eudragit S (examples 36, 37; see also § 444).

The seal coating in D1 improves the stability of the active ingredient with respect to moisture (see e.g. §§ 275, 391). It is explicitly stated that the seal coating provides insulation from moisture and protection from chemical degradation (§ 275).

Claim 1 differs from D1, in that the coating comprises waxes or wax derivatives.

In view of D1, the problem to be solved by claim 1 is to provide an improved water-resistant coated formulation.

Claim 1 is considered inventive. Although waxes are listed as exemplary seal coat materials (see § 278), it is not obvious from D1 that waxes would provide an improved water resistance with respect to other seal coats listed. Indeed in the examples of D1 other seal coatings are used.

5 - Mutatis mutandis the same arguments apply to the other independent claims.

Industrial Applicability

6 - Claims 1-77 and 81-85 fulfill the requirements of Article 33(4) PCT (see also Item III).

Re Item VI

Certain documents cited

Certain published documents

Application No Patent No	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date *(valid claim)* *(day/month/year)*
WO2004/009085A	29/1/04	17/7/03	19/7/02

CLAIMS:

1. A pharmaceutically acceptable oral formulation comprising core material which comprises a therapeutically effective amount of a 5-HT-receptor agonist, or a pharmaceutically acceptable salt, solvate or derivative thereof, which core material is provided with a substantially water resistant coating comprising one or more substantially water resistant materials, wherein said one or more substantially water resistant materials comprise one or more waxes, or one or more wax derivatives.

2. A pharmaceutically acceptable oral formulation according to claim 1, wherein said 5-HT-receptor agonist is selected from the group consisting of sumatriptan, zolmitriptan, naratriptan and rizatriptan, and pharmaceutically acceptable salts, solvates and derivatives thereof.

3. A pharmaceutically acceptable oral formulation according to claim 2, wherein said 5-HT-receptor agonist is sumatriptan, or a pharmaceutically acceptable salt or solvate thereof.

4. A pharmaceutically acceptable oral formulation according to claim 3, wherein said 5-HT-receptor agonist is sumatriptan succinate.

5. A pharmaceutically acceptable oral formulation according to any of claims 1 to 4, which is substantially free of degradation products associated with exposure of a 5-HT-receptor agonist to ambient moisture.

6. A pharmaceutically acceptable oral formulation according to claims 4 and 5, which is a tablet formulation including 25mg of sumatriptan succinate, and wherein there is present under storage conditions of about 1 month at 25EC and 60% relative humidity, less than about 0.60% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide.

7. A pharmaceutically acceptable oral formulation according to claim 6, wherein there is present under storage conditions of about 1 month at 25EC and 60% relative humidity, less than about 0.55% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide.

8. A pharmaceutically acceptable oral formulation according to claim 7, wherein there is present under storage conditions of about 1 month at 25EC and 60% relative humidity, about 0.50% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide.

9. A pharmaceutically acceptable oral formulation according to claims 4 and 5, which is a tablet formulation including 25mg of sumatriptan succinate, and wherein there is present under storage conditions of about 1 month at 40EC and 75% relative humidity, less than about 0.65% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide.

10. A pharmaceutically acceptable oral formulation according to claim 9, wherein there is present under storage conditions of about 1 month at 40EC and 75% relative humidity, less than about 0.60% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide.

11. A pharmaceutically acceptable oral formulation according to claim 10, wherein there is present under storage conditions of about 1 month at 40EC and 75% relative humidity, about 0.55% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide.

12. A pharmaceutically acceptable oral formulation according to claims 4 and 5, which is a tablet formulation including 100mg of sumatriptan succinate, and wherein there is present under storage conditions of about 1 month at 25EC and 60% relative humidity, less than about 0.60% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide.

13. A pharmaceutically acceptable oral formulation according to claim 12, wherein there is present under storage conditions of about 1 month at 25EC and 60% relative humidity, less than about 0.55% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide.

14. A pharmaceutically acceptable oral formulation according to claim 13, wherein there is present under storage conditions of about 1 month at 25EC and 60% relative humidity, about 0.50% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide.

15. A pharmaceutically acceptable oral formulation according to claims 4 and 5, which is a tablet formulation including 100mg of sumatriptan succinate, and wherein there is present under storage conditions of about 1 month at 40EC and 75% relative humidity, less than about 0.65% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide.

16. A pharmaceutically acceptable oral formulation according to claim 15, wherein there is present under storage conditions of about 1 month at 40EC and 75% relative humidity, less than about 0.60% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide.

17. A pharmaceutically acceptable oral formulation according to claim 16, wherein there is present under storage conditions of about 1 month at 40EC and 75% relative humidity, about 0.55% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide.

18. A tablet formulation comprising core material which comprises a therapeutically effective amount of sumatriptan succinate, together with a substantially water resistant coating provided to said core material and comprising one or more waxes, or one or more wax derivatives, characterised in that said tablet formulation contains about 25mg of sumatriptan succinate and under storage conditions of about 1 month at 25EC and 60% relative humidity, less than about 0.60% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide is present in the tablet formulation.

19. A tablet formulation according to claim 18, wherein less than about 0.55% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide is present in the tablet formulation, under storage conditions of about 1 month at 25EC and 60% relative humidity.

20. A tablet formulation according to claim 19, wherein about 0.50% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide is present in the tablet formulation, under storage conditions of about 1 month at 25EC and 60% relative humidity.

21. A tablet formulation comprising core material which comprises a therapeutically effective amount of sumatriptan succinate, together with a substantially water resistant coating provided to said core material and comprising one or more waxes, or one or more wax derivatives, characterised in that said tablet formulation contains about 25mg of sumatriptan succinate and under storage conditions of about 1 month at 40EC and 75%

relative humidity, less than about 0.65% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide is present in the tablet formulation.

22. A tablet formulation according to claim 21, wherein less than about 0.60% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide is present in the tablet formulation, under storage conditions of about 1 month at 40EC and 75% relative humidity.

23. A tablet formulation according to claim 22, wherein about 0.55% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide is present in the tablet formulation, under storage conditions of about 1 month at 40EC and 75% relative humidity.

24. A tablet formulation comprising core material which comprises a therapeutically effective amount of sumatriptan succinate, together with a substantially water resistant coating provided to said core material and comprising one or more waxes, or one or more wax derivatives, characterised in that said tablet formulation contains about 100mg of sumatriptan succinate and under storage conditions of about 1 month at 25EC and 60% relative humidity, less than about 0.60% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide is present in the tablet formulation.

25. A tablet formulation according to claim 24, wherein less than about 0.55% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide is present in the tablet formulation, under storage conditions of about 1 month at 25EC and 60% relative humidity.

26. A tablet formulation according to claim 25, wherein about 0.50% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-

indol-5-yl]-N-methylmethanesulphonamide is present in the tablet formulation, under storage conditions of about 1 month at 25EC and 60% relative humidity.

27. A tablet formulation comprising core material which comprises a therapeutically effective amount of sumatriptan succinate, together with a substantially water resistant coating provided to said core material and comprising one or more waxes, or one or more wax derivatives, characterised in that said tablet formulation contains about 100mg of sumatriptan succinate and under storage conditions of about 1 month at 40EC and 75% relative humidity, less than about 0.65% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide is present in the tablet formulation.

28. A tablet formulation according to claim 27, wherein less than about 0.60% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide is present in the tablet formulation, under storage conditions of about 1 month at 40EC and 75% relative humidity.

29. A tablet formulation according to claim 28, wherein about 0.55% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide is present in the tablet formulation, under storage conditions of about 1 month at 40EC and 75% relative humidity.

30. A formulation according to any preceding claim, wherein said wax is selected from the group consisting of beeswax, shellac, carnauba wax, spermaceti, lanolin, jojoba oil, candellila wax, ozocerite and opaglos 6000 P.

31. A formulation according to claim 30, wherein said wax is selected from the group consisting of carnauba wax, beeswax and opaglos 6000 P.

32. A formulation according to any of claims 1 to 31, wherein said substantially water-resistant coating further comprises one or more coating excipient materials, solvents for the waxes and plasticizers to coat solid formulations.

33. A formulation according to any of claims 1 to 32, wherein said substantially water-resistant coating is directly applied to the core material.

34. A formulation according to any of claims 1 to 33, wherein core material comprises sumatriptan succinate, mannitol or dibasic calcium phosphate or calcium carbonate, hypromellose and / or microcrystalline cellulose, croscarmellose sodium and magnesium stearate.

35. A formulation according to claim 34, wherein core material comprises sumatriptan succinate, mannitol, hypromellose and / or microcrystalline cellulose, croscarmellose sodium and magnesium stearate.

36. A formulation according to claim 34, wherein core material comprises sumatriptan succinate, dibasic calcium phosphate, hypromellose and / or microcrystalline cellulose, croscarmellose sodium and magnesium stearate.

37. A formulation according to claim 34, wherein core material comprises sumatriptan succinate, calcium carbonate, hypromellose and / or microcrystalline cellulose, croscarmellose sodium and magnesium stearate.

38. A formulation according to claim 34, which comprises about 20 to 55 % w/w sumatriptan succinate, about 20 to 50 % w/w mannitol or dibasic calcium phosphate or calcium carbonate, about 1 to 10% w/w hypromellose and / or microcrystalline cellulose, about 1 to 5 % w/w croscarmellose sodium and about 0.5 to 2 % w/w magnesium stearate.

39. A formulation according to claim 38, which comprises about 20 to 55 % w/w sumatriptan succinate, about 20 to 50 % w/w mannitol, about 1 to 10% w/w hypromellose

and / or microcrystalline cellulose, about 1 to 5 % w/w croscarmellose sodium and about 0.5 to 2 % w/w magnesium stearate.

40. A formulation according to claim 38, which comprises about 20 to 55 % w/w sumatriptan succinate, about 20 to 50 % w/w dibasic calcium phosphate, about 1 to 10% w/w hypromellose and / or microcrystalline cellulose, about 1 to 5 % w/w croscarmellose sodium and about 0.5 to 2 % w/w magnesium stearate.

41. A formulation according to claim 38, which comprises about 20 to 55 % w/w sumatriptan succinate, about 20 to 50 % w/w calcium carbonate, about 1 to 10% w/w hypromellose and / or microcrystalline cellulose, about 1 to 5 % w/w croscarmellose sodium and about 0.5 to 2 % w/w magnesium stearate.

42. Use of one or more waxes, or one or more wax derivatives, to inhibit degradation of a 5-HT-receptor agonist susceptible to degradation on exposure to ambient moisture, wherein said one or more waxes, or one or more wax derivatives, provides a substantially water resistant coating to a core material comprising a 5-HT-receptor agonist, or a pharmaceutically acceptable salt, solvate or derivative thereof, of a pharmaceutically acceptable oral formulation.

43. Use according to claim 42, wherein said 5-HT-receptor agonist is selected from the group consisting of sumatriptan, zolmitriptan, naratriptan and rizatriptan, and pharmaceutically acceptable salts, solvates and derivatives thereof.

44. Use according to claim 43, wherein said 5-HT-receptor agonist is sumatriptan, or a pharmaceutically acceptable salt or solvate thereof.

45. Use according to claim 44, wherein said 5-HT-receptor agonist is sumatriptan succinate.

46. Use according to claim 45, where said formulation comprises a tablet formulation including 25mg of sumatriptan succinate, and inhibition of said degradation products is

such that there is present in said tablet formulation less than about 0.60% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide, under storage conditions of about 1 month at 25EC and 60% relative humidity.

47. Use according to claim 46, wherein inhibition of said degradation products is such that there is present in said tablet formulation less than about 0.55% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide, under storage conditions of about 1 month at 25EC and 60% relative humidity.

48. Use according to claim 46, wherein inhibition of said degradation products is such that there is present in said tablet formulation about 0.50% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide, under storage conditions of about 1 month at 25EC and 60% relative humidity.

49. Use according to claim 45, where said formulation comprises a tablet formulation including 25mg of sumatriptan succinate, and inhibition of said degradation products is such that there is present in said tablet formulation less than about 0.65% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide, under storage conditions of about 1 month at 40EC and 75% relative humidity.

50. Use according to claim 49, wherein inhibition of said degradation products is such that there is present in said tablet formulation less than about 0.60% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide, under storage conditions of about 1 month at 40EC and 75% relative humidity.

51. Use according to claim 50, wherein inhibition of said degradation products is such that there is present in said tablet formulation about 0.55% by weight of [3-[2-

(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide, under storage conditions of about 1 month at 40EC and 75% relative humidity.

52. Use according to claim 45, where said formulation comprises a tablet formulation including 100mg of sumatriptan succinate, and inhibition of said degradation products is such that there is present in said tablet formulation less than about 0.60% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide, under storage conditions of about 1 month at 25EC and 60% relative humidity,.

53. Use according to claim 52, wherein inhibition of said degradation products is such that there is present in said tablet formulation less than about 0.55% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide, under storage conditions of about 1 month at 25EC and 60% relative humidity.

54. Use according to claim 53, wherein inhibition of said degradation products is such that there is present in said tablet formulation about 0.50% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide, under storage conditions of about 1 month at 25EC and 60% relative humidity.

55. Use according to claim 45, where said formulation comprises a tablet formulation including 100mg of sumatriptan succinate, and inhibition of said degradation products is such that there is present in said tablet formulation less than about 0.65% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide under storage conditions of about 1 month at 40EC and 75% relative humidity.

56. Use according to claim 55, wherein inhibition of said degradation products is such that there is present in said tablet formulation less than about 0.60% by weight of [3-[2-

(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide, under storage conditions of about 1 month at 40EC and 75% relative humidity.

57. Use according to claim 56, wherein inhibition of said degradation products is such that there is present in said tablet formulation about 0.55% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide under storage conditions of about 1 month at 40EC and 75% relative humidity.

58. Use according to any of claims 42 to 57, wherein said wax is selected from the group consisting of beeswax, shellac, carnauba wax, spermaceti, lanolin, jojoba oil, candellila wax, ozocerite and opaglos 6000 P.

59. Use according to claim 58, wherein said wax is selected from the group consisting of carnauba wax, beeswax and opaglos 6000 P.

60. A method of substantially inhibiting the formation, in a pharmaceutically acceptable oral formulation, of degradation products associated with exposure of a 5-HT-receptor agonist to ambient moisture, which method comprises providing core material comprising a 5-HT-receptor agonist, or a pharmaceutically acceptable salt, solvate or derivative thereof, with a substantially water resistant coating comprising one or more substantially water resistant materials, wherein said one or more substantially water resistant materials comprise one or more waxes, or one or more wax derivatives.

61. A method according to claim 60, wherein said 5-HT-receptor agonist is selected from the group consisting of sumatriptan, zolmitriptan, naratriptan and rizatriptan, and pharmaceutically acceptable salts, solvates and derivatives thereof.

62. A method according to claim 61, wherein said 5-HT-receptor agonist is sumatriptan, or a pharmaceutically acceptable salt or solvate thereof.

63. A method according to claim 62, wherein said 5-HT-receptor agonist is sumatriptan succinate.

64. A method according to claim 63, where said formulation comprises a tablet formulation including 25mg of sumatriptan succinate, and inhibition of said degradation products is such that there is present in said tablet formulation less than about 0.60% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide, under storage conditions of about 1 month at 25EC and 60% relative humidity.

65. A method according to claim 64, wherein inhibition of said degradation products is such that there is present in said tablet formulation less than about 0.55% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide, under storage conditions of about 1 month at 25EC and 60% relative humidity.

66. A method according to claim 65, wherein inhibition of said degradation products is such that there is present in said tablet formulation about 0.50% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide, under storage conditions of about 1 month at 25EC and 60% relative humidity.

67. A method according to claim 63, where said formulation comprises a tablet formulation including 25mg of sumatriptan succinate, and inhibition of said degradation products is such that there is present in said tablet formulation less than about 0.65% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide, under storage conditions of about 1 month at 40EC and 75% relative humidity.

68. A method according to claim 67, wherein inhibition of said degradation products is such that there is present in said tablet formulation less than about 0.60% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-

indol-5-yl]-N-methylmethanesulphonamide, under storage conditions of about 1 month at 40EC and 75% relative humidity.

69. A method according to claim 68, wherein inhibition of said degradation products is such that there is present in said tablet formulation about 0.55% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide, under storage conditions of about 1 month at 40EC and 75% relative humidity.

70. A method according to claim 63, where said formulation comprises a tablet formulation including 100mg of sumatriptan succinate, and inhibition of said degradation products is such that there is present in said tablet formulation less than about 0.60% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide, under storage conditions of about 1 month at 25EC and 60% relative humidity.

71. A method according to claim 70, wherein inhibition of said degradation products is such that there is present in said tablet formulation less than about 0.55% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide, under storage conditions of about 1 month at 25EC and 60% relative humidity.

72. A method according to claim 71, wherein inhibition of said degradation products is such that there is present in said tablet formulation about 0.50% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide, under storage conditions of about 1 month at 25EC and 60% relative humidity.

73. A method according to claim 63, where said formulation comprises a tablet formulation including 100mg of sumatriptan succinate, and inhibition of said degradation products is such that there is present in said tablet formulation less than about 0.65% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-

yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide under storage conditions of about 1 month at 40EC and 75% relative humidity.

74. A method according to claim 73, wherein inhibition of said degradation products is such that there is present in said tablet formulation less than about 0.60% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide, under storage conditions of about 1 month at 40EC and 75% relative humidity.

75. A method according to claim 74, wherein inhibition of said degradation products is such that there is present in said tablet formulation about 0.55% by weight of [3-[2-(dimethylamino)ethyl]-2-[[3-[2-(dimethylamino)ethyl]-1H-indol-5-yl]methyl]-1H-indol-5-yl]-N-methylmethanesulphonamide under storage conditions of about 1 month at 40EC and 75% relative humidity.

76. A method according to any of claims 60 to 75, wherein said wax is selected from the group consisting of beeswax, shellac, carnauba wax, spermaceti, lanolin, jojoba oil, candellila wax, ozocerite and opaglos 6000 P.

77. A method according to claim 76, wherein said wax is selected from the group consisting of carnauba wax, beeswax and opaglos 6000 P.

78. A method of treating a condition prevented, ameliorated or eliminated by administration of a 5-HT-receptor agonist, which method comprises administering to a human patient suffering from or susceptible to such a condition a therapeutically effective amount of a formulation according to any of claims 1 to 41.

79. A method according to claim 78, wherein said condition being treated is selected from the group consisting of migraine, cluster headache, chronic paroxysmal hemicrania, headache associated with vascular disorders, tension headache and paediatric migraine.

80. A method according to claim 79, wherein said condition is migraine.

81. Use of a therapeutically effective amount of a 5-HT-receptor agonist present in a core material, or a pharmaceutically acceptable salt, solvate or derivative thereof, and a substantially water resistant coating for said core material comprising one or more substantially water resistant materials, in the manufacture of a formulation according to any of claims 1 to 41, for the treatment of a condition prevented, ameliorated or eliminated by administration of a 5-HT-receptor agonist.

82. Use according to claim 81, wherein said condition being treated is selected from the group consisting of migraine, cluster headache, chronic paroxysmal hemicrania, headache associated with vascular disorders, tension headache and paediatric migraine.

83. Use according to claim 82, wherein said condition is migraine.

84. A process of preparing a pharmaceutically acceptable oral formulation according to any of claims 1 to 41, which process comprises providing core material which comprises a therapeutically effective amount of a 5-HT-receptor agonist, or a pharmaceutically acceptable salt, solvate or derivative thereof, and providing the core material with a substantially water resistant coating comprising one or more substantially water resistant materials, wherein said one or more substantially water resistant materials comprise one or more waxes; or one or more wax derivatives.

85. A process according to claim 84, which employs wet granulation or direct compression techniques.